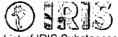


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## 1,1,2-Trichloroethane (CASRN 79-00-5)

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Reference Dose for Chronic Oral Exposure (RfD)



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#### 1,1,2-Trichloroethane; CASRN 79-00-5

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR 1,1,2-Trichloroethane

#### File First On-Line 03/31/1987

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	02/01/1995
Inhalation RfC Assessment (I.B.)	no data	12/01/1992
Carcinogenicity Assessment (II.)	on-line	02/01/1994

#### I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

#### \_I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name -- 1,1,2-Trichloroethane CASRN -- 79-00-5 Last Revised -- 02/01/1995

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of

Chronic Health Hazards for Non-Carcinogenic Effects

Reference Dose for Chronic Oral Exposure (RfD)

- Oral RfD Summary
- Principal and Supporting Studies
- Uncertainty and
- Modifying Factors Additional Studies/
- Comments
- Confidence in the Oral RfD
- **EPA Documentation** and Review

Reference Concentration for Chronic Inhalation Exposure (RfC)

- Inhalation RfC Summary
- Principal and
- Supporting Studies
- Uncertainty and
- **Modifying Factors** Additional Studies/
- Comments Confidence in the Inhalation RfC
- **EPA Documentation** and Review

Carcinogenicity Assessment for Lifetime Exposure

Evidence for Human Carcinogenicity

- Weight-of-Evidence Characterization
- <u>Human</u>
- Carcinogenicity Data Animal Carcinogenicity Data
- Supporting Data for Carcinogenicity



substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

Quantitative Estimate of Carcinogenic Risk from Oral Exposure

#### I.A.1. Oral RfD Summary

**Critical Effect Experimental Doses\*** RfD UF MF Clinical serum NOAEL: 20 mg/L (drinking 1000 4E-3 - 1 water) (3.9 mg/kg/day) chemistry mg/kg/day

Mouse Subchronic LOAEL: 200 mg/L (drinking **Drinking Water Study** water) (44 mg/kg/day)

White et al., 1985 Sanders et al., 1985

- Summary of Risk **Estimates**
- Dose-Response Data Additional Comments
- Discussion of Confidence

Quantitative Estimate of Carcinogenic Risk from Inhalation **Exposure** 

- Summary of Risk Estimates
- Dose-Response Data
- **Additional Comments**
- Discussion of Confidence

EPA Documentation, Review and, Contacts

- Revision History Synonyms
- Bibliography

\*Conversion Factors: None

#### \_I.A.2. Principal and Supporting Studies (Oral RfD)

Sanders, V.M., K.L. White, Jr., G.M. Shopp, Jr. and A.E. Munson. 1985. Humoral and cell-mediated immune status of mice exposed to 1,1,2- trichloroethane. Drug Chem. Toxicol. 8(5): 357-372.

White, K.L., Jr., V.M. Sanders, V.W. Barnes, G.M. Shopp, Jr. and A.E. Munson. 1985. Toxicology of 1,1,2-trichloroethane in the mouse. Drug Chem. Toxicol. 8(5): 333-355.

The studies by White et al. (1985) and Sanders et al. (1985) have been selected as the basis for the derivation of the oral RfD because they are adequate studies in which mice of both sexes were exposed to 1,1,2- trichloroethane in drinking water for 90 days. Concentrations provided were 0, 20, 200, or 2000 mg/L, which resulted in intakes of 0, 4.4, 46, and 305 mg/kg/day for males and 0, 3.9, 44, and 384 mg/kg/day for females. Clinical chemistry indications of adverse effects on the liver occurred in both sexes at 2000 mg/L. Effects on the erythrocytes occurred only in females and depressed humoral immune status occurred in both sexes at 200 and 2000 mg/L. The concentration of 20 mg/L, corresponding to 3.9 mg/kg/day for female rats, (White et al., 1985; Sanders et al., 1985) is the NOAEL at which significant adverse effects were not observed and is chosen as the basis for the derivation of an oral RfD.

#### I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF -- The UF includes the standard uncertainty factors for interspecies and intrahuman variability, and a factor of 10 for extrapolation to lifetime exposure from an intermediate exposure duration.

MF -- None

#### I.A.4. Additional Studies/Comments (Oral RfD)

The previous oral RfD (2E-1 mg/kg/day) was based on the NCI (1978) study in rats. This study's major weakness was its lack of reporting of noncancer effects. Also, doses far below the NCI (1978) NOAEL (65.7 mg/kg/day) have been shown to alter levels of clinical serum chemistries, which are indicative of systemic tissue damage.

#### I.A.5. Confidence in the Oral RfD

Study -- Medium Database -- Medium RfD -- Medium

The critical study is given a medium confidence for balanced strengths (clinical chemistries) and weaknesses (lack of histopathology and a NOAEL). The supporting database and the RfD are rated medium because of the general lack of appropriate chronic toxicologic data.

#### I.A.6. EPA Documentation and Review of the Oral RfD

U.S. EPA. 1987. Drinking Water Health Advisory for 1,1,2-Trichloroethane. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. ECAO-CIN-W027.

U.S. EPA. 1980. Ambient Water Quality Criteria for Chlorinated Ethanes. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Washington, DC. EPA 440/5-80-029. NTIS PB 81- 117400.

Agency Work Group Review -- 12/18/1985, 05/15/1986, 05/26/1988

Verification Date -- 05/26/1988

Screening-Level Literature Review Findings -- A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for 1,1,2-Trichloroethane conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at <a href="https://hotline.iris@epa.gov">hotline.iris@epa.gov</a> or 202-566-1676.

#### \_\_I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or <a href="https://hotline.iris@epa.gov">hotline.iris@epa.gov</a> (internet address).

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#### \_I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name -- 1,1,2-Trichloroethane CASRN -- 79-00-5

Not available at this time.

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#### \_II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name -- 1,1,2-Trichloroethane CASRN -- 79-00-5 Last Revised -- 02/01/1994

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10.000, 1 in 100.000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

#### \_II.A. Evidence for Human Carcinogenicity

#### II.A.1. Weight-of-Evidence Characterization

Classification -- C; possible human carcinogen

Basis -- Hepatocellular carcinomas and pheochromocytomas in one strain of mice forms the basis for this classification. Carcinogenicity was not shown in rats. 1,1,2-Trichloroethane is structurally related to 1,2-dichloroethane, a probable human carcinogen.

#### \_\_II.A.2. Human Carcinogenicity Data

None

#### \_\_II.A.3. Animal Carcinogenicity Data

In a bioassay conducted by NCI (1978) technical grade (92.7% pure) 1,1,2-trichloroethane was administered by gavage in corn oil to Osborne-Mendel rats and B6C3F1 mice: (50/species/sex/dose) for each of 2 doses and 20 animals/species/sex for each of 2 control groups. Administration was 5 times/week for 78 weeks during which time doses for rats were increased from 70 and 30 mg/kg/ day to 100 and 50 mg/kg/day and doses for mice were increased from 300 and 150 mg/kg/day to 400 and 200 mg/kg/day. By two statistical tests, treatment of mice was found to be associated with increased incidence of hepatocellular carcinomas. A dose-related increase in pheochromocytomas was also confirmed in female mice. Tumors found in treated but not control rats included adrenal cortical carcinomas; transitional-cell carcinomas of kidney; renal tubular adenomas; and hemangiosarcomas of spleen, pancreas, abdomen and subcutaneous tissue. There was, however, no statistically significant increase in tumor incidence in rats as a function of treatment.

#### II.A.4. Supporting Data for Carcinogenicity

1,1,2-Trichloroethane was found to be nonmutagenic for Salmonella typhimurium (Simmon et al., 1977). In rats and mice acutely exposed to 1,1,2-trichloroethane by inhalation and intraperitoneal injection, trichloroacetic acid, trichloroethanol, chloroacetic acid and thiodiacetic acid were among the urinary metabolites identified

(Yllner, 1971; Ikeda and Ohtsuji, 1972). 1,1,2-Trichloroethane is structurally related to 1,2- dichloroethane, a probable human carcinogen.

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## \_II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

#### II.B.1. Summary of Risk Estimates

Oral Slope Factor -- 5.7E-2 per (mg/kg)/day

Drinking Water Unit Risk -- 1.6E-6 (ug/L)

Extrapolation Method -- Linearized multistage procedure, extra risk

Drinking Water Concentrations at Specified Risk Levels:

Risk Level	Concentration	
E-4 (1 in 10,000)	6E+1 ug/L	
E-5 (1 in 100,000)	6E+0 ug/L	
E-6 (1 in 1,000,000)	6E-1 ug/L	

#### II.B.2. Dose-Response Data (Carcinogenicity, Oral Exposure)

Tumor Type -- hepatocellular carcinoma Test Animals -- Mouse/B6C3F1 Route -- gavage Reference -- NCI, 1978

Administered Dose (mg/kg)/day	Human Equivalent Dose (mg/kg)/day	Tumor Incidence
0	0	2/20
139	9.3	18/49
279	18.6	37/49

#### \_\_II.B.3. Additional Comments (Carcinogenicity, Oral Exposure)

Doses are TWAs adjusted for frequency of exposure (5/7 days). Weight of the mice was assumed to be 0.033 kg.

The unit risk should not be used if the water concentration exceeds 6E+3 ug/L, since above this concentration the unit risk may not be appropriate.

#### \_\_II.B.4. Discussion of Confidence (Carcinogenicity, Oral Exposure)

Dose-related increases in hepatocellular carcinomas were observed in adequate numbers or mice of both sexes. Background incidence of this tumor type is generally high. Modeling was done on only one data set.

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II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

### \_\_II.C.1. Summary of Risk Estimates

Inhalation Unit Risk -- 1.6E-5 per (ug/cu.m)

Extrapolation Method -- Linearized multistage procedure, extra risk

Air Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	6E+0 ug/cu.m
E-5 (1 in 100,000)	6E-1 ug/cu.m
E-6 (1 in 1,000,000)	6E-2 ug/cu.m

#### \_\_II.C.2. Dose-Response Data for Carcinogenicity, Inhalation Exposure

This inhalation risk estimate was calculated from the oral exposure data in Section II.B.2.

#### \_\_II.C.3. Additional Comments (Carcinogenicity, Inhalation Exposure)

The unit risk should not be used if the air concentration exceeds 6E+2 ug/cu.m, since above this concentration the unit risk may not be appropriate.

#### \_\_II.C.4. Discussion of Confidence (Carcinogenicity, Inhalation Exposure)

See II.B.4.

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## \_II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

#### \_\_II.D.1. EPA Documentation

Source Document -- U.S. EPA, 1980

The values in the Ambient Water Quality Criteria Document for Chlorinated Ethanes received extensive peer and public review.

#### II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review -- 07/23/1986

Verification Date -- 07/23/1986

Screening-Level Literature Review Findings -- A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer

assessment for 1,1,2-Trichloroethane conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at <a href="mailto:hotline.iris@epa.gov">hotline.iris@epa.gov</a> or 202-566-1676.

#### \_\_II.D.3. EPA Contacts (Carcinogenicity Assessment)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or <a href="https://hotline.iris@epa.gov">hotline.iris@epa.gov</a> (internet address).

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#### \_VI. Bibliography

\_III. [reserved] \_IV. [reserved] \_V. [reserved]

Substance Name -- 1,1,2-Trichloroethane CASRN -- 79-00-5 Last Revised -- 08/01/1990

#### VI.A. Oral RfD References

NCI (National Cancer Institute). 1978. Bioassay of 1,1,2-trichloroethane for possible carcinogenicity. U.S. DHEW Tech. Rep. Ser. 74. Publ. No. NIH 78-1324.

Sanders, V.M., K.L. White, Jr., G.M. Shopp, Jr. and A.E. Munson. 1985. Humoral and cell-mediated immune status of mice exposed to 1,1,2- trichloroethane. Drug Chem. Toxicol. 8(5): 357-372.

U.S. EPA. 1980. Ambient Water Quality Criteria for Chlorinated Ethanes. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Washington, DC. EPA 440/5-80-029. NTIS PB 81-117400.

U.S. EPA. 1987. Drinking Water Health Advisory for 1,1,2-Trichloroethane. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. ECAO-CIN-W027.

White, K.L., Jr., V.M. Sanders, D.W. Barnes, G.M. Shopp, Jr. and A.E. Munson. 1985. Toxicology of 1,1,2-trichloroethane in the mouse. Drug Chem. Toxicol. 8(5): 333-355.

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#### VI.B. Inhalation RfC References

None

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#### \_VI.C. Carcinogenicity Assessment References

Ikeda, M. and H. Ohtsuji. 1972. A comparative study of the excretion of Fujiwara reaction-positive substances in urine of humans and rodents given trichloro- or tetrachloro-derivatives of ethane and ethylene. Brit. J. Industr. Med. 29: 99-104.

NCI (National Cancer Institute). 1978. Bioassay of 1,1,2-trichloroethane for possible carcinogenicity. U.S. DHEW Tech. Rep. Ser. 74. Publ. No. NCI-CG-TR- 74.

Simmon, V.F., K. Kauhanon and R.G. Tardiff. 1977. Mutagenic activity of chemicals identified in drinking water. In: Progress in Genetic Toxicology, D. Scott et al., Ed. Elsevier/North Holland Biomedical Press, Amsterdam. p. 249-258.

Yllner, S. 1971. Metabolism of 1,1,2-Trichloroethane - 1,2-14C in the mouse. Acta Pharmacol. et Toxicol. 30: 248-256. From the National Institute of Occupational Health, Stockholm, Sweden.

U.S. EPA. 1980. Ambient Water Quality Criteria for Chlorinated Ethanes. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Washington, DC. EPA 440/5-80-029. NTIS PB 81-117400.

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#### VII. Revision History

Substance Name -- 1,1,2-Trichloroethane CASRN -- 79-00-5

Date	Section	Description
09/30/1987	IV.	Regulatory Action section on-line
03/01/1988	II.B.4.	Confidence statement revised
03/01/1988	II.C.4.	Confidence statement revised
09/26/1988	I.A.	Oral RfD replaced
03/01/1990	I.B.	Inhalation RfC now under review
06/01/1990	IV.F.1.	EPA contact changed
06/01/1990	VI.	Bibliography on-line
08/01/1990	I.A.	Text edited
08/01/1990	11.	Text edited
08/01/1990	III.A.	Health Advisory on-line
08/01/1990	VI.D.	Health Advisory references added
01/01/1991	II.	Text edited
01/01/1991	II.C.1.	Inhalation slope factor removed (global change)
01/01/1992	I.A.7.	Secondary contact changed
01/01/1992	IV.	Regulatory actions updated
12/01/1992	I.B.	Work group review date added

02/01/1994	II.D.3.	Secondary contact's phone number changed
02/01/1995	I.A.7.	Secondary contact's name changed
08/01/1995	I.B.	EPA's RfD/RfC and CRAVE workgroups were discontinued in May, 1995. Chemical substance reviews that were not completed by September 1995 were taken out of IRIS review. The IRIS Pilot Program replaced the workgroup functions beginning in September, 1995.
04/01/1997	III., IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.
10/28/2003	I.A.6, II.D.2	Screening-Level Literature Review Findings message has been added.

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#### \_VIII. Synonyms

Substance Name -- 1,1,2-Trichloroethane CASRN -- 79-00-5 Last Revised -- 03/31/1987

79-00-5
ETHANE TRICHLORIDE
ETHANE, 1,1,2-TRICHLORONCI-C04579
RCRA WASTE NUMBER U227
RCRA WASTE NUMBER U359
beta-T
1,1,2-TRICHLORETHANE
1,1,2-Trichloroethane
1,2,2-TRICHLOROETHANE
Trichloroethane, 1,1,2beta-TRICHLOROETHANE
TROJCHLOROETHANE
TROJCHLOROETAN(1,1,2)
VINYL TRICHLORIDE

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